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CASE REPORT

Vibrio vulnificus and *V. parahaemolyticus* necrotising fasciitis in fishermen visiting an estuarine tropical northern Australian location

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Summary Three cases of severe necrotising fasciitis due to *Vibrio vulnificus* (two cases) and *Vibrio parahaemolyticus* (one case, fatal), have occurred in Caucasian tourists while fishing at a remote tropical northern Australian estuarine area. Infections were acquired over a 4-year period during the tourist fishing season (April to July 2000–2003), when water temperatures range from 23 to 30 °C. They are notable for their geographical clustering in the remote western aspect of the Gulf of Carpentaria, an area characterised by sedimentary stratiform zinc-lead-silver deposits and a major mining operation. Patients presented with classical bullous cellulitis with necrotising fasciitis, accompanied by severe sepsis. Underlying risk factors were identified in each patient; in one instance, previously unrecognised haemochromatosis was diagnosed. Likely reasons for *Vibrio* occurrence in this particular ecological niche are discussed.

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Introduction

Infections caused by marine *Vibrio* species arise due to a combination of specific favourable environmental and

host factors. In Australia, sporadic and infrequent cases of infection due to *V. vulnificus*, *V. parahaemolyticus*, *V. damsela*, *V. alginolyticus*, and non-01 *V. cholerae* have been reported in the literature.^{1–8} These include only two recognised cases of serious infection from the north of Australia, comprising fatal non-01 *V. cholerae* sepsis, in Aboriginal patients from the Kimberley region of North Western Australia.⁸ Mandatory laboratory reporting of *Vibrio* food poisoning in the Northern Territory has detected four cases over the last 7 years. The three cases reported

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here, and an additional fourth recently described case from the same locality,¹⁰ demonstrate an apparent emerging geographical focus (Fig. 1) for acquisition of *Vibrio* infections in the Northern Territory.

Case 1

A 55 year old man with alcoholic cardiomyopathy, chronic liver disease and chronic airways disease, presented in July 2000 with septic shock and severe blistering leg cellulitis. The left leg was dusky and dark red below the knee, with fluid-filled blisters and areas of necrotic skin. The toe had first become swollen 3 days prior, after he had been catching fish and prawns in a tidal river (Site 1, Fig. 1).

On arrival he was shocked and had acute renal failure with creatinine of 259 $\mu\text{mol/L}$ (normal range 60–120 $\mu\text{mol/L}$). Initial treatment included ticarcillin plus clavulanate, clindamycin, inotropes, non-invasive ventilation, and continuous veno-venous haemofiltration. Within 24 h of hospitalisation, guillotine amputation of the leg was required as the limb was no longer viable. Gram stain of intraoperative tissue demonstrated Gram negative bacilli, which were identified as *V. vulnificus*. Antimicrobial therapy was changed to intravenous doxycycline and ceftazidime (Fig. 2). He was managed in the intensive care unit for 20 days, and required extensive rehabilitation thereafter. He died of his underlying co-morbidities 2 years later.

Case 2

In May 2001, a 63 year old man with type 2 diabetes, congestive cardiac failure, atrial fibrillation (for which he was warfarinised), chronic airways disease, and a lower limb ulcer (present for approximately 1 week), went fishing

in seawater with his legs fully immersed (Site 3, Fig. 1). Approximately 12 h later, he required emergency transfer to hospital with delirium, septic shock, transient myocardial ischaemia, acute renal failure, pancytopenia, hypoglycaemia, coffee-grounds vomitus and an exquisitely tender, swollen, red left lower leg.

He was treated initially with cephazolin, gentamicin, metronidazole, dextrose, noradrenaline and morphine, and was transferred to the intensive care unit for ongoing inotropic support and continuous veno-venous filtration. Gram stain of fluid aspirated from the left foot revealed Gram negative rods. Antibiotics were changed to meropenem, gentamicin and doxycycline 200 mg intravenously twice daily.

The limb was urgently debrided, with removal of necrotic fascia from the left shin and dorsum of the right foot. *V. parahaemolyticus* was isolated from the initial aspirates, and from intraoperative tissue specimens. Blood cultures were sterile. The post-operative course was complicated by progressive renal failure, liver dysfunction and gastrointestinal bleeding. He died 18 days later due to multi-organ failure.

Case 3

A 38 year old man with no past medical history presented in April 2003 with an exquisitely painful, swollen lower limb, fever and hypotension. The foot had become painful and swollen on the second day of a fishing holiday. He had visited two locations (Site 2, Fig. 1) by boat, and his legs had frequent contact with water. Symptoms progressed rapidly, such that on arrival in hospital 24 hours later, multiple large bullae were seen extending from the foot to the upper medial thigh, with mottling and swelling of

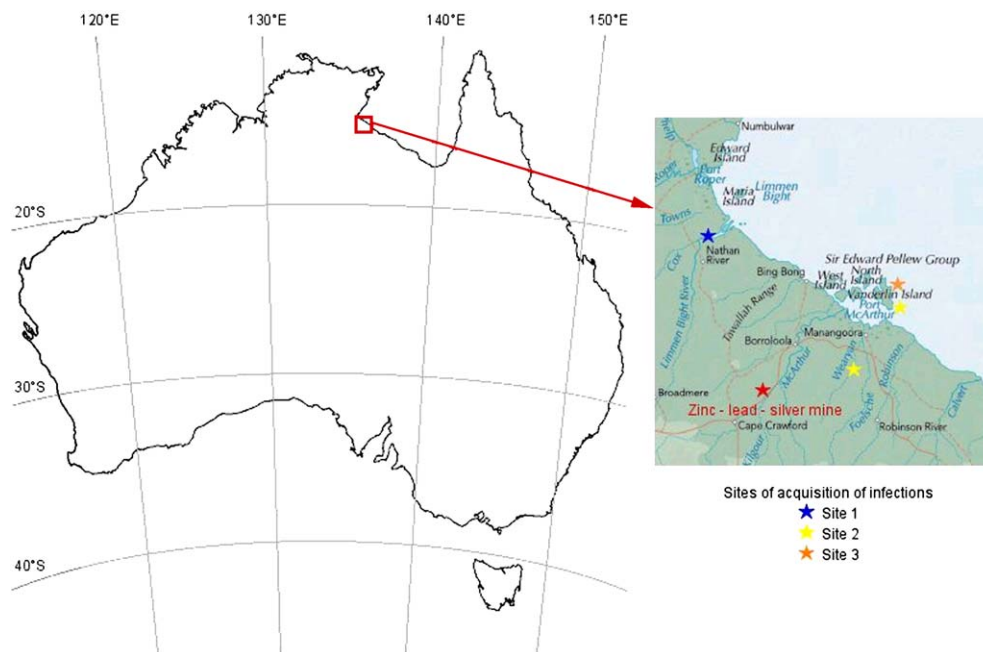


Figure 1 Map of Australia showing sites of acquisition of *Vibrio* infections. Borroloola township geographic details: latitude (degrees south): -16.0667 ; longitude (degrees east): 136.3000 .



Figure 2 Blistering cellulitis and necrotising fasciitis due to *V. vulnificus*. (A) Case 1, prior to amputation; (B) and (C) Case 3, pre-debridement; (D) Case 3, post-debridement.

surrounding tissue. He was mildly pancytopenic and coagulopathic, with acute renal failure and mildly abnormal liver function.

Vibrio infection was suspected clinically, and he was treated with intravenous doxycycline 100 mg twice daily and meropenem after obtaining blood and blister fluid for culture. The leg was urgently debrided from the dorsum of the left foot to the groin. *V. vulnificus* was isolated

from blister fluid and intraoperative tissue specimens. The leg was debrided 24–48 hourly for the next 10 days. Left forefoot amputation was required on day 6 of admission due to peripheral gangrene. The illness was complicated by myocardial infarction and refractory hypertension. Split skin grafting of the limb was undertaken a month later, and the patient made a full recovery.

Investigation was made of underlying risk factors. There was no evidence of diabetes, but iron studies were found to be grossly abnormal (ferritin >30 000 µg/L (normal range 15–200 µg/L), iron 28 µmol/L (normal range 12–27 µmol/L), transferrin 0.99 g/L (normal range 2.0–3.6 g/L), total iron binding capacity 25 µmol/L (normal range 42–76 µmol/L), saturation ratio 1.13 (normal range 0.2–0.5)). He was subsequently found to be homozygous for the C282Y gene mutation, consistent with haemochromatosis. He had no known family history of haemochromatosis, and once sepsis had resolved, he had no evidence of impaired hepatic function or other end-organ involvement. Cardiac function also returned to normal as documented echocardiographically.

Discussion

These cases are typical of *V. vulnificus* and *V. parahaemolyticus* necrotising fasciitis clinically, epidemiologically and geographically. *Vibrio* infection associated with high morbidity and mortality therefore needs to be considered in visitors to this area, and appropriate public health warnings provided to those at risk. Infection with *Vibrio* sp. may be the defining event leading to the diagnosis of an underlying risk factor, as in the instance of haemochromatosis in Case 3. The history of sea water contact and the bullous appearance assist in differentiating from other causes of necrotising fasciitis, such as Group A Streptococci (GAS). GAS necrotising fasciitis occurs at elevated frequency in the Top End of the Northern Territory (incidence 3.8 per 100 000 general population; 5.8 per 100 000 in the indigenous population), in keeping with the high community prevalence of GAS infection and post infectious sequelae.⁹

During preparation of this manuscript, a fourth case of *Vibrio* infection has occurred in the same locality. Markey¹⁰ reports that a 19 year old indigenous female, treated with oral steroids for autoimmune hepatitis, complicated by cirrhosis and portal hypertension, presented with overwhelming sepsis and died within 24 h of illness onset, after swimming in a tidal river in same vicinity as these cases. Non-toxicogenic *V. cholerae* was isolated from her blood cultures.

The geographical clustering of these cases of unusual infection is particularly notable given the small number of visitors annually to this remote coastal location. Although water conditions seem favourable for *Vibrio* growth throughout much of Australia's northern waters, it would appear that a local environmental factor must specifically favour *Vibrio* growth in this region. Aspects of marine climate conducive for *Vibrio* growth include appropriate temperature, salinity, pH and the presence of zooplanktons.^{11–14} Despite these stipulations, *Vibrio* species are characterised by their ability to adapt to altered marine environments, such as polluted waterways.¹³ This ability to evolve in accordance with external pressure is likely

related in part to the presence of a superintegron, in a process analogous to the development of antibiotic resistance by organisms under antibiotic pressure. This has been demonstrated in soil organisms found in an area contaminated by heavy-metal containing mine tailings.¹⁵ The orebody in this northern Australian location is said to be one of the largest known deposits of zinc and lead in the world. Concentrations of zinc and lead in the river downstream from the mine have been noted to be twice the levels recorded upstream, and as high as 100 µg/L early in the wet season (three times the 80th percentile Australian and New Zealand Environment Conservation Council water quality trigger values). Other heavy metals including copper are similarly found in high concentration downstream.¹⁶ These levels are likely to be diluted in the further downstream estuarine regions where the *Vibrio* infections occurred, although actual heavy metal concentrations in this area are unknown.

On exposure of the host to the organism, the internal host milieu is similarly important in determining the ongoing survival of *Vibrio*. Specifically, iron overload, as demonstrated in Case 3, and likely present also in Case 1 as a consequence of alcoholic liver disease, provides a permissive environment for *V. vulnificus* proliferation, since the organism is impaired in its ability to extract iron from transferrin.¹⁷ Improved survival of *V. vulnificus* therefore occurs in blood with higher ferritin concentration and transferrin iron saturation.^{17,18} The influence of environmental heavy metals on *Vibrio* growth *ex vivo* is less well described. It would appear that zinc at least is among its important constitutive minerals, as zinc-containing metalloproteases, contributing to pathogenic potential, are elaborated by *Vibrio*.¹⁹ A link between *Vibrio* infections and local environmental perturbation is speculative only, but it would appear possible that altered heavy metal water content in the area could have the potential to affect *Vibrio* population density and hence risk of human infection.

The epidemiology of infection with environmental organisms will continue to evolve in the current era of climate change,²⁰ as both small and large scale influences alter local microbial ecology, and bring about changes in the patterns of human–pathogen interactions.^{21,22} Understanding microbial environmental growth requirements is therefore important not only in explaining current patterns of disease occurrence, but in anticipating future change.

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